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Procedia Engineering 44 (2012) 307 – 309

Procedia Engineering

www.elsevier.com/locate/procedia

Euromembrane Conference 2012

[OB47]

Potential of organic solvent nanofiltration in continuous catalytic reactions

L. Peeva*, A. Livingston

Imperial College London, UK

Introduction

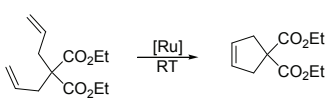
Complex organic molecules, such as active pharmaceutical ingredients, are typically synthesized by multiple reactions, involving metal-organic catalysts and it is often necessary for substrates to pass through several reaction and separation steps. One approach for eliminating some of these steps is the use of multifunctional catalyst systems, however, this is not an easy solution with homogeneous organometallic catalysts, since coordination chemistry is normally quite different between the metals to be used. Usually, when two or more homogeneous organometallic catalysts are mixed together, they would lower their respective performance by some negative interactions [1]. Flow chemistry represents an attractive solution for multi-step synthesis not only for its established advantages but also for the possibility of carrying out two or more reactions with no or minimal workup and purification [2]. Continuous flow techniques can often provide better mixing and heat transfer, precise control over concentrated or hazardous reaction streams, reduced solvent waste and synthetic shortcuts together with rapid process optimisation of synthetic steps on a small scale [3].

Organic solvent nanofiltration is an emerging technology for performing membrane separation/purification processes in organic solvents and has been successfully applied for metal-organic catalysts recovery [4]. One major advantage of the OSN separation is that it does not require any phase transition or biphasic operation. Thus the development of continuous catalytic process combined with continuous catalyst recovery by OSN could offer major economic and process efficiency advantages over the conventional batch-based system and/or biphasic operation processes

This work demonstrates a continuous ring closing metathesis (RCM) reaction where Ru catalyst is retained by a polymeric OSN membrane. The process was operated in two modes - continuous stirred tank reactor mode (CSTR) and plug flow reactor mode (PFR).

The RCM reaction

To prove the concept a model RCM reaction that forms a stable product is the most appropriate. The RCM of diethyl diallylmalonate (**Scheme 1)** was selected and carried out.



Scheme 1: Model RCM reaction of diethyl diallylmalonate.

Membrane screening

Four commercially available membranes were selected for this investigation Starmem 228, Starmem 240, Duramem 500 and Puramem 280. The screening was performed in a dead end cell by filtering a RCM postreaction mixture through the membranes and measuring the catalyst

doi:10.1016/j.proeng.2012.08.397

and product rejections. The initial screening suggested that Starmem 228 and Puramem 280 are showing the best performance in terms of rejection and membrane stability and were used for further investigations.

Continuous RCM reaction combined with OSN membrane separation

A flow-through nanofiltration unit with working volume of ~60 ml and membrane area of 51 cm^2 was set up and used for continuous reaction-separation experiments. In order to improve the catalyst retention a POSS enlarged Ru catalyst was selected. The reaction was performed in 120 ml toluene at 40^0C. Initially the reaction was performed in a separate flask for 2.5 hours to reach completion before being loaded in continuous mode (CSTR). The catalyst seems to show high reactivity and after 2.5 hours ~84% conversion was achieved. The post reaction mixture was loaded in a continuous mode system (CSTR) and fresh feed at very low dilution rate 0.2 ml min^{-1} (residence time 600 minutes) was supplied. The commercial membrane PuraMem280 was used to retain the catalyst. The permeate was colourless suggesting good retention of the catalyst. The reaction ran for ~2000 minutes and although a decrease in conversion was observed the catalyst showed good productivity. The catalyst losses (based on Ru in the permeate) were low ~1.8% overall for the run. Due to the manual control of the equipment we were unable to run the process for longer however this result is promising and further continuous reaction operations are needed to evaluate the process feasibility.

Finally the catalyst was investigated in continuous mode using plug-flow reactor configuration (**Figure 1**) where the catalyst and the feed were supplied as two separate streams. The 40 ml plug-flow reactor ran continuously for 32 hours showing a stable conversion of ~100% throughout the run. The permeate stream contained ~0.34 mgL^{-1} Ru suggesting ~0.2% catalyst losses. Apparently the plug-flow configuration seemed the most promising and further investigation should be performed in order to evaluate its through potential.

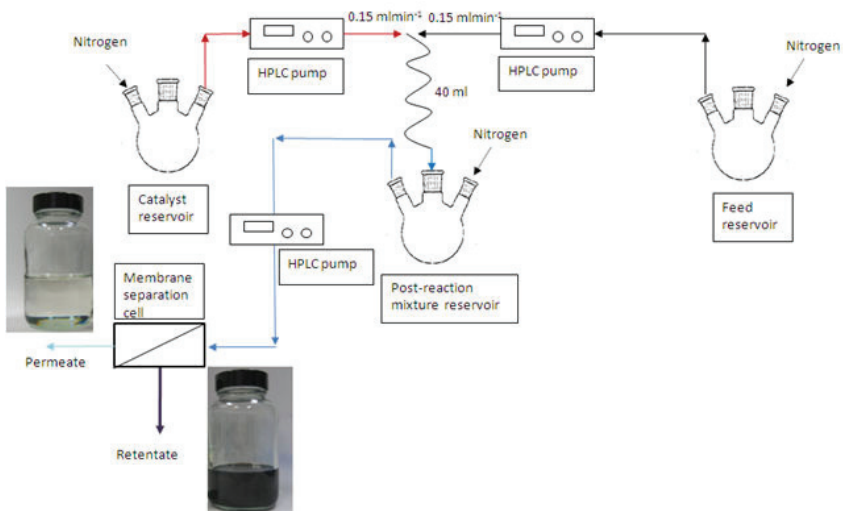


Figure 1 Schematic representation of the plug-flow reactor process scheme for the continuous metathesis reaction.

Conclusions

A continuous RCM reaction was successfully performed in a flow-through nanofiltration membrane reactor/separator unit in CSTR and PFR modes. The plug-flow configuration seemed the most promising and further investigation should be performed in order to evaluate its through potential.

Acknowledgement

This work was funded by the FP7-NMP-2007-SMALL-1Grant NoCP-FP 214095-2 HiCAT project.

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Keywords: organic solvent nanofiltration, catalytic reactions, continuous